growth (as a proxy for rupture risk and the need for repair) were examined.

Results: The average radiologic follow-up time was 22.0 ± 13.6 months and the average aneurysm growth rate was 2.8 ± 1.7 mm/year. PWS in VWT models significantly differed from PWS in UWT models (238 ± 68 vs 212 ± 73 kPa; $P = .025$). In our sample, initial aortic diameter was not found to be correlated with aneurysm growth ($r = .26$; $P = .19$). A stronger correlation was found between aneurysm growth and PWS derived from VWT models as compared to PWS from UWT models ($r = .86$ vs $r = .58$; $P = .032$ by Fisher's r to Z transformation; Fig).

Conclusions: The inclusion of locally variable wall thickness significantly improved the correlation between PWS and aneurysm growth. Aortic wall thickness should be incorporated into future FEA models to accurately predict clinical outcomes.

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PS172.

A20 Increases eNOS Expression and Activity to Sustain Endothelial Cell Function Under Inflammatory Insults

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Objectives: Nitric oxide generated by endothelial nitric oxide synthase (eNOS) acts at different levels to sustain proper endothelial cell (EC) function. Pro-inflammatory molecules associated with various pathological conditions negatively affect eNOS expression and activity, altering vascular homeostasis. Decreased eNOS levels and activity are the pathognomonic features of EC dysfunction and a prelude to atherosclerotic remodeling of the vasculature. We have demonstrated that A20 maintains EC homeostasis by inhibiting NF-kappa B activation and protecting from apoptosis. The aim of this study is to explore whether A20 impacts eNOS expression/activity.

Methods: A20 was overexpressed in human coronary artery EC (HCAEC) by recombinant adenovirus-mediated gene transfer. Effects of A20 on eNOS expression and phosphorylation were analyzed by quantitative PCR, human eNOS promoter-luciferase reporter assay, chromatin immunoprecipitation (ChIP) and Western blot.

Results: Our data demonstrate that over-expression of A20 in HCAEC significantly increased eNOS mRNA and protein levels by promoting eNOS transcription, as demonstrated by ChIP, and eNOS promoter analysis using Luciferase reporter assays. Importantly, A20-induced upregulation of eNOS expression was sustained in HCAEC treated with tumor necrosis factor that inhibits eNOS transcription and function. Moreover, A20 enhanced phosphorylation of eNOS (Ser-1177), a surrogate marker of its activity, by promoting the activation of its upstream kinase AKT.

Conclusions: Our data demonstrate that A20 upregulates and activates eNOS, even in EC exposed to inflammation. A20's ability to promote and sustain eNOS activity could be critical to its cytoprotective effect in EC. Further, it supports our pursuit of A20-based therapies to maintain vascular homeostasis, preventing vascular diseases such as atherosclerosis, transplant arteriosclerosis and diabetic vasculopathy.

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PS174.

Hypertension and Other Cardiovascular Risk Factors Lead to Premature Rarefaction of the Native Collateral Circulation

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Objectives: Collaterals are an important determinant of the capacity for compensation in occlusive disease. In mice, advanced age (>16 months-age) is accompanied by anatomic loss, or rarefaction, of native (pre-existing) collaterals, resulting in worse ischemic injury. Targeted deletion of eNOS greatly accelerates collateral loss, implicating eNOS deficiency in age-associated collateral rarefaction. To determine whether other CV risk factors in addition to aging that are known to associate with eNOS deficiency also cause collateral rarefaction, we examined 7-8 months-old mice with hypertension (renin transgene; MAP 139 ± 3 mmHg) and other genetically imposed CV risk factors.

Methods: Functional assessment of collateral capacity in skeletal muscle was obtained by measurement of hindlimb perfusion, limb use and ischemic appearance scores after femoral artery ligation, and in brain by determining infarct volume after middle cerebral artery occlusion. Collateral extent (number and diameter) was determined by filling the arterial circulation with a silicone-based casting agent (Microfil™).

Results: Hypertensive mice had greater reduction in hindlimb flow immediately after ligation (depends on native collateral extent) and impaired recovery of perfusion during 21 days thereafter (depends on native extent plus collateral remodeling), worse ischemia and use impairment, increased cerebral infarct volume, reduced native collateral extent, and impaired collateral remodeling. Mice with metabolic syndrome showed similar collateral rarefaction and functional impairments. In contrast, hyperlipidemia, type-1 diabetes and obesity were not accompanied by collateral rarefaction.

Conclusions: Chronic hypertension leads to rarefaction of the native collateral circulation and worse ischemia and tissue necrosis following acute arterial obstruction. Ongoing experiments are examining the molecular mechanisms underlying hypertension-induced collateral rarefaction.

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